UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,734	10/06/2000	Ib Mendel-Hartvig	10806-129	1611

24256 7590 09/09/2003

DINSMORE & SHOHL, LLP
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI, OH 45202

EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/09/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/582,734	Applicant(s) MENDEL-HARTVIG ET AL.	
	Examiner Gary W. Counts	Art Unit 1641	

-- The MAILING DATE of this communication app ars on th cover sh et with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the claims

In view of the Appeal Brief filed on June 27, 2003, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Rejections Withdrawn

1. Claim 12 stand withdrawn from rejection under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to claim 12 filed February 24, 2003 in paper number 12, thus gave greater clarity to the claim.

2. Applicant's arguments, see Appeal Brief, filed June 27, 2003, with respect to the recitation "adapted" in claim 18 have been fully considered and are persuasive. The 112 second paragraph rejection concerning the recitation "adapted" of claim 18 has been withdrawn.

3. Applicant's arguments, see Appeal Brief, filed June 27, 2003, with respect to claims 2, 8, 19 and 23 that Dafforn et al fails to teach Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix have been fully considered and are persuasive. The 102 rejections of claims 2, 8, 18 and 23 have been withdrawn.

4. Applicant's arguments, see Appeal Brief, filed June 27, 2003, with respect to claim 33 that Dafforn et al fails to teach a calibrator, or any binder for a calibrator, or for providing a calibrator in kit form with a device as defined in claim 18 have been fully considered and are persuasive. The 102 rejection of claim 33 has been withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4 and 6-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because part A) recites that an application zone contains buffer and sample then part C) recites the addition of the liquid with sample. It is unclear if the sample added in part C) is the same sample that the application zone contains in part A) or if the sample is different. Further, it is unclear why sample is added to an application zone which already contains sample.

Claim 1 is vague and indefinite because part (II) refers to LZ_m as a zone, but part (b) of claim 1 defines m as the total number of zones. It is unclear if m is an actual zone or if it refers to the number of zones. Therefore, the inconsistency between m being a zone or the number of zones renders the claim indefinite.

Claim 1 part b), is vague and indefinite because it is unclear whether the limitation ($m \geq 2$) contained within the parenthesis are part of the claimed invention. See also deficiency found in part b), claim 18.

Claim 1 part II, is vague and indefinite because it is unclear whether the limitation "$m \neq n$" contained within the parenthesis are part of the claimed invention. See also deficiency found in part e), claim 18.

Claim 2 is vague and indefinite because it is unclear whether the limitation "sequential variants regarding analyte and Reactant*" contained within the parenthesis are part of the claimed invention.

Claim 3 is vague and indefinite because it is unclear whether the limitation "simultaneous variants regarding analyte and Reactant*" contained within the parenthesis are part of the claimed invention.

Claim 6 the recitation "wherein LZ_{n+1} finishes where LZ_n starts" is vague and indefinite. It is unclear what finishes. Is flowing finished or is flowing finished out of the zone? Or is applicant insinuating that the one application zone is connected to another? It is unclear what applicant intends. See also deficiency found in claim 22.

Claim 6 is vague and indefinite because it is unclear whether the limitation "m≠n" contained within the parenthesis are part of the claimed invention. See also deficiency found in claim 22.

Claim 11 the recitation "transported components" is vague and indefinite. It is unclear what applicant is referring to (i.e. Reactant*, analyte, buffer or is applicant referring to something else? There is no definition or guidance provided for the phrase in the specification.

Claim 11 is vague and indefinite because it is unclear whether the limitations "LZ_{n+1} and LZ_{n-1}" contained within the parenthesis are part of the claim.

Claim 13 the recitation "$m \leq 6$ is vague and indefinite because claim 1 requires that $m \geq 2$. Claim 1 recites that there are at least two application zones. Instantly recited claim 13 encompasses that m can be 1. However, this contradicts claim 1. See also deficiency in claim 27 which contradicts claim 18.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 3, 7, 9, 10, 13, 14, 18, 20, 21, 24, 25, 27, 28 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Dafforn et al (US 4,981,786).

Dafforn et al disclose an immunoassay device and method for determining an analyte in a sample. Dafforn et al also disclose that the device comprises a bibulous material which is susceptible to traversal by an aqueous medium in response to capillary force (flow matrix), (col 7, lines 8-10). Dafforn et al disclose that the device may be used in assays wherein absorbent material is utilized to assist the flow of liquid

away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 10-16). Dafforn et al disclose the device comprises a first means for introducing a sample into the device and second means other than the first means for introducing a liquid reagent other than the sample into the device (col 3, lines1-20). Dafforn et al disclose that the liquid reagent can be an ancillary reagent such as a buffer or a labeled reagent (Reactant*). Dafforn et al disclose that the labeled reagent can be provided as liquid reagent or predeposited (col 19, line 15 – col 20, line 22). Dafforn et al disclose that the liquid reagent can be added upstream of the test solution (sample) (col 18, lines 27-29). Dafforn et al also disclose that both of these application zones are located upstream of a immunosorbing zone (detection zone) and that specific binding members (antibodies) (Reactant I) are immobilized in the immunosorbing zone (col 18, line 3 – col 19, line 48). Dafforn et al disclose that the strip may be coated with a material (col 19, lines 1-9). Dafforn et al disclose that the device contains dividers (spacers) between the first means and second means. Dafforn et al also disclose that the sample may be introduced before the liquid reagent if so desired (col 18, lines 20-32). Dafforn et al disclose that the contact portion can also serve as the immunsorbing zone (detection zone) or separate immunosorbing zones can be utilized depending on the particular assay protocol chosen (col 18, lines 45-48). Dafforn et al also disclose that the application of liquid can be performed simultaneously in the application zones (col 24, lines 30-32). Dafforn et al also disclose that the reagents can be predeposited in the matrix. Dafforn et al also disclose packaging the components into a kit.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 2, 4, 6, 8, 11, 19, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al (US 4,981,786).

See above for teachings of Dafforn et al.

Dafforn et al differ from the instant invention in failing to specifically teach n">n' wherein Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix.

Dafforn et al is silent with respect to substantially simultaneously adding Reactant*, upstream of liquid application zone for sample. However, Dafforn et al specifically teach that the Reactant* can be applied upstream of the liquid application zone for sample. Dafforn et al also disclose many embodiments regarding Reactant* in which Reactant* is applied upstream of the application zone of sample or to the same zone as the sample. Although, Dafforn teaches that when (Reactant*) is added upstream of sample, that the liquid reagent usually is added following the addition of sample (col 13, lines 32-44), Dafforn also teaches the addition of liquid reagents simultaneously (col 24). Therefore, it would have been obvious to one of ordinary skill in the art to add Reactant* upstream of a liquid application zone for sample and to apply the liquids simultaneously in order to optimize assay conditions. Further, it is well settled that a reference must be evaluated for all disclosures not just its preferred embodiments. *In re Mills,* 470 F. 2d 649, 176 USPQ 196 (CCPA 1972).

8. Claims 12, 15, 16, 26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al in view of Robinson et al (WO 95/16914).

See above for teachings of Dafforn et al.

Dafforn et al differ from the instant invention in failing to disclose the matrix comprising at least one calibrator zone, in which calibrator is bound.

Robinson et al disclose the use of calibration zone(s), in which a calibration reagent is immobilized and has biospecific affinity for the analyte of interest or the binding partner of interest (page 15, lines 15-24). Robinson et al also disclose a releasable reagent predeposited (abstract). Robinson et al also disclose that the device may be a flow through device such as test strip (page 5, lines 7-22).

Robinson et al also disclose that the specific binding partner can be coupled to or conjugated to the calibrator (see page 17), to form a complex for detection. Robinson et al disclose that the reagents may be antigen/antibody complexes. Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-16) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed (page 14, lines 24-26).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a calibrator zone as taught by Robinson et al into the method and device of Dafforn et al because Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-16) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed.

9. Claims 17 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al in view of Self et al (US 4,446,231).

See above for teachings of Dafforn et al.

Dafforn et al and differ from the instant invention in failing to teach the diagnosis of an autoimmune disease.

Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune diseases. Self et al shows that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

It would have been obvious to one of ordinary skill in the art to use immunoassays as taught by Self et al for the diagnosis of autoimmune diseases because Self et al shows that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Therefore it would have been obvious to one of ordinary skill in the art to use the device and method of Dafforn et al for diagnosing autoimmune disease.

Response to Arguments

Applicant's arguments filed June 27, 2003 have been fully considered but they are not persuasive.

102 rejections

Applicant argues that Dafforn et al provide no teaching or suggestion relating to simultaneous application with a sequential flow of reagents through a matrix. This is not

found persuasive because Dafforn et al specifically teach that sample and liquid can be added simultaneously to two different application zones and that the sample is located downstream of the liquid. One skilled in the art would recognize that if the liquid reagent is added to an application zone (i.e. Figure 1, well 22) and sample is added to a separate application zone (i.e. Figure 1, well 20) simultaneously that they would both contact the flow matrix almost simultaneously and since the sample is located downstream of the liquid reagent, the liquid reagent would be transported through the matrix immediately after the sample.

Applicant argues that in contrast, Dafforn et al teach that the developer solution applied at a second opening carries a complex of HCG applied at a first opening and enzyme conjugate to the detection zone, i.e., the liquids applied simultaneously at the first and second openings mix prior to their travel to the detection zone and the upstream liquid is not transported through the matrix immediately after liquid added to the nearest downstream application zone. This is not found persuasive because regardless if the developer is added or not the complex will flow toward the detection zone. As disclosed by Dafforn absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or regents for analyzing for the analyte (col 4, lines 12-16). Therefore, when sample is applied to application zone downstream of liquid reagent, the sample begins to migrate and therefore even when the sample and liquid reagent are added simultaneously the sample would flow in front of liquid reagent. Further, if the complex and developer as disclosed in Dafforn are carried together and

mix the reaction would occur before the detection zone. Dafforn clearly states (col 24, lines 35-37) that the reaction occurs at the detection zone. Therefore, the complex binds to the immobilized antibody and then the developer reacts to produce a color change. Thus, Dafforn reads on the instantly recited claims.

Applicant argues that according to claims 10 and 24, the zones $LZ_m..LZ_n..LZ_1$ have zone spacers between each other. And as described in the specification, the zone spacers are one manner in which the sequential transport of substantially simultaneously applied liquids may be obtained and wherein zone spacers in the form of strips are provide to form spaced liquid application zones to which liquids may be applied simultaneously via a multichannel pipette. Applicant argues that Dafforn et al does not teach such spacers. This is not found persuasive because Dafforn et al clearly states that the device contains dividers (spacers) between the first means and second means. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., wherein zone spacers in the form of strips are provided to form spaced liquid application zones to which liquids may be applied simultaneously via a multichannel pipette) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, Dafforn reads on the instantly recited claims.

103 rejections

Applicant argues that Robinson et al does not teach or suggest employing any of the elements of Robinson et al's sensor in the multiple port assay device of Dafforn et al and that there is no teaching or suggestion for modifying the teachings of Dafforn et al to include any portion of the Robinson et al teachings particularly those which would relate to calibration zones, calibrator and binder. This is not found persuasive because Robinson et al clearly disclose (page 5, lines 7-15) that the device can be a test strip (same device as Dafforn) and Robinson clearly states that advantages of using calibration zones and calibration reagents (page 3, lines 15-16 and page 14, lines 24-26). Therefore, it is the Examiner's position that the combination of Dafforn et al and Robinson et al is proper and thus the rejection maintained.

Applicant argues that Self does not teach or suggest a device for determination of an analyte in a sample and a flow matrix employing a combination of biospecfic affinity reactants and liquid applications zones and flow as defined in claims 1 and 18 and that applicant's find no teaching or suggestion by Self for modifying any of the teachings of Dafforn et al to result in either a method or a device as presently claimed. This is not found persuasive because Examiner has not relied upon self for the determination of an analyte in a sample and a flow matrix employing a combination of biospecfic affinity reactants and liquid applications zones and flow but rather has relied upon Dafforn for these teachings. Further, Dafforn et al specifically teach that the device may be utilized in any number of assay wherein absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for

analyzing for the analyte (col 4, lines 11-16). Further, Dafforn et al disclose that the device can be used to detect autoimmune antibodies and antibodies to allergens (col 5, lines 1-6). Since, Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune disease. It is the Examiner's position that It would have been obvious to one of ordinary skill in the art to combine the teachings of Dafforn et al and Self et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
August 27, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
08/21/03